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## **REMARKS**

Applicants respectfully request reconsideration of the application in view of the foregoing amendments and the following remarks.

Claims 1-3, 5-10, 18, and 19 are canceled herein without prejudice to pursuing the subject matter of said claims in a further continuing application.

Claims 4, 11, and 13 have been amended to more particularly point out and distinctly claim the subject matter of Applicants' invention. Support for these amendments can be found, for example, in Figures 1-3.

It is believed that the current amendment places the application in condition for allowance. Applicants respectfully note that claims drawn to nucleic acid sequences encoding the amino acid sequences of the present invention issued as U.S. Patent 5,840,306.

## Sequence Requirements

The application was objected to for failure to comply with requirements for patent applications containing nucleotide sequence disclosures as set forth in 37 C.F.R. §§ 1.821 – 1.825. Specifically, the Office Action states that Applicants must provide (1) an initial or substitute paper copy of the Sequence Listing, as well as an amendment directing entry into the specification, (2) an initial or substitute Sequence Listing in Computer Readable Form (CRF), and (3) a statement that the content of the paper and CRF are the same and add no new matter.

In response thereto, Applicants submit herewith a paper Sequence Listing, a Sequence Listing in Computer Readable Form, and a statement that the content of the paper and CRF are the same and add no new matter, in fulfillment of the requirements of 37 CFR §§ 1.821 through 1.825 (sent to "Box Sequence," copies of paper Sequence Listing and Statement enclosed). Applicants respectfully request entry of the Sequence Listing into the Specification.

## Restriction Requirement

The Office Action states that restriction to one of the following inventions is required under 35 U.S.C. §§ 121 and 372:

- Group I, Claims 1-3, 8, 10, drawn to isolated, purified DNA molecule.
- Group II, Claim 4, drawn to purified protein.
- Group III, Claim 5, drawn to antibodies.
- Group IV, Claims 6, 7, drawn to process for expression of human papillomavirus type 18 in host

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• Group V, Claim 9, drawn to vaccine for prevention or treatment of human papillomavirus

- Group VI, Claims 11, 12, 15, 16, 17, 20, drawn to virus like particles, vaccine, composition, and method of preventing papillomavirus infection.
- Group VII, Claim 13, drawn to method of producing virus like particles.
- Group VIII, Claim 14, drawn to recombinant papillomavirus protein.
- Group IX, Claim 18, drawn to method of producing yeast derived recombinant capsid protein.
- Group X, Claim 19, drawn to virus like particles.

By way of this response, Applicants respectfully traverse the restriction requirement set forth above. Specifically, Applicants request the regrouping of Groups II, VI, VII, and VIII into a single group for reasons set forth below. However, in order to comply with the restriction requirement, Applicants provisionally elect Group VI, claims 11, 12, 15, 16, 17, and 20, without prejudice to the prosecution of the non-elected claims in related patent applications. Applicants also provisionally elect the HPV18 L1 amino acid sequence (SEQ ID NO:2) for examination on the merits, as reflected in amended claims 4 and 11.

The Office Action states that the inventions listed in Groups I-X do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The Office Action further states that said special technical feature is lacking because the invention of Group I is known in the prior art.

Applicants note that the claims, as amended, are drawn to an essentially purified HPV18 L1 protein comprising a novel sequence of amino acids as set forth in SEQ ID NO:2 (claim 4) and virus-like particles comprising this novel L1 sequence, either alone or in combination with a specific HPV18 L2 sequence (claim 11). All other pending claims depend from claim 11.

The HPV18 L1 nucleotide and corresponding amino acid sequences of the present invention represent novel, synthetic consensus sequences derived from sequencing HPV18 derived from clinical isolates (see Examples 4 and 5). Surprisingly, Applicants found that the sequences identified all suggested the same amino acid changes to the published sequence. Since the clones obtained in the present application were derived from clinical isolates, it is concluded that they, rather than the published HPV18 L1 amino acid sequence, actually reflect the predominant viral sequences associated with clinical infections. Therefore, the L1 protein disclosed herein is much more appropriate to form the basis of a vaccine since it will make, with

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or without L2 protein, more authentic VLPs and thus will elicit more appropriate antibodies than VLPs based on the previously published sequence.

As such, Applicants respectfully submit that the pending claims do in fact possess the requisite special technical "linking" feature because Applicants novel sequence makes a significant contribution over the prior art. Accordingly, reconsideration and withdrawal of the requirement for restriction and/or regrouping of the claims, e.g., by combining Groups II, VI, VII, and VIII is respectfully requested.

## Summary

Applicants respectfully submit that all claims are in condition for allowance and a favorable action on the merits is earnestly solicited. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of the case.

Respectfully submitted,

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